exo-5-dimethylamino-5,6-dihydro-*exo*-dicyclopentadiene, 18530-64-8; amine oxide of *exo*-5-dimethylamino-5,6-dihydro-*exo*-dicyclopentadiene, 18530-65-9.

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Absolute Configurations and Rotations of 1-Methyl-2-methylenenorbornane and 1,2-Dimethyl-2-norbornyl Derivatives

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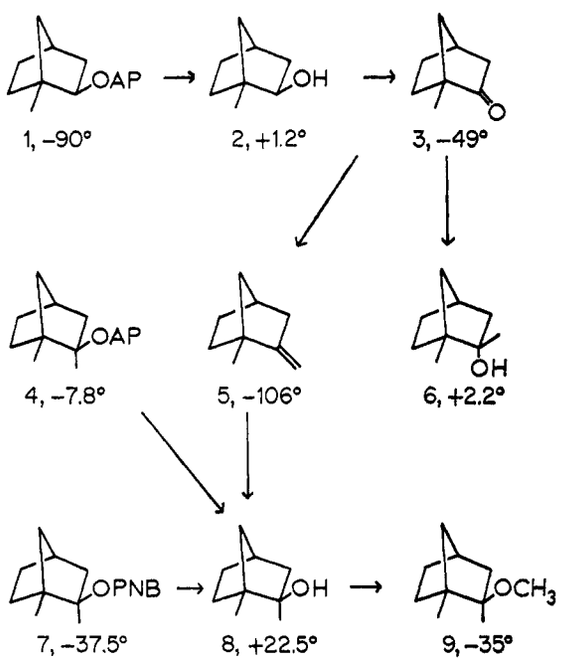
Absolute configurations of 1-methyl-2-methylenenorbornane (**5**) and *exo*- (**8**) and *endo*-1,2-dimethyl-2-norbornanol (**6**) have been established by correlation with 1-methyl-2-norboranone (**3**). The correlations also provide absolute rotations for these compounds. Optical resolutions of the 1-methyl-*exo*-2-norbornyl and 1,2-dimethyl-*exo*-2-norbornyl systems are described.

In connection with an investigation of the solvolysis of optically active 1,2-dimethyl-*exo*-2-norbornyl *p*-nitrobenzoate (**7**)[1] we have had occasion to relate configurations and rotations of optically active 1,2-dimethyl-*exo*-2-norbornyl derivatives (**4** and **7**–**9**) and 1-methyl-2-methylenenorbornane (**5**). Configurations and rotations were correlated as outlined in Chart I. The absolute configuration of (−)-1-methyl-2-norbornanone (**3**) had been established earlier[2] by correlation with (−)-fenchone. The present correlations establish absolute configurations for the compounds included in Chart I.

CHART I



1-Methyl-*exo*-2-norbornanol (**2**) was prepared from norcamphor as described earlier[2] and the acid phthalate derivative, **1**, was resolved by recrystallization of the cinchonine salt. The most active sample of **1** was found to be about 40% optically pure by the correlation outlined below.

Saponification of (−)-1-methyl-*exo*-2-norbornyl acid phthalate (**1**), followed by oxidation (CrO_3) of the resulting (+) **2** by a method that has been shown[3] to convert *exo*-2-norbornanol into norcamphor with complete preservation of optical configuration, gave (−)-1-methyl-2-norbornanone (**3**). To avoid optical fractionation the intermediate solid (+) **2** was not isolated. An independent saponification was used to relate the rotations of **1** and **2**.

The ketone, (−) **3**, was converted into (+)-1,2-dimethyl-*endo*-2-norbornanol (**6**) by reaction with methylmagnesium bromide and into (−)-1-methyl-2-methylenenorbornane (**5**) by the Wittig reaction. Oxymercuration–demercuration of (−) **5** according to the method outlined by Brown and coworkers[4] gave (+)-1,2-dimethyl-*exo*-2-norbornanol (**8**). It has been shown[4] that oxymercuration–demercuration of 1-methyl-d_3-2-methylenenorbornane gives 1-methyl-d_3-2-methyl-*exo*-norbornanol without detectable scrambling of the methyl groups and from this, and the reproducible change in rotation for the conversion of active **5** to **8**, it seems that this step proceeds without loss of optical activity.

The rotations included in the chart[5] result from correlation with the highest observed rotations for the 1,2-dimethyl-*exo*-2-norbornyl derivatives. This correlation gives a rotation for 1-methyl-2-norbornanone (**3**) that is about 15% higher than that obtained[2] by correlation with *d*-fenchone. This discrepency could result from partial loss of activity for the two-step conversion of **3** into **8**. However, for reasons given above this seems unlikely. The changes in rotation for each step of the conversion of active **1** into active **8** were found to be reproducible by different investiga-

(1) H. L. Goering and K. Humski, *J. Amer. Chem. Soc.*, **90**, 6213 (1968).
(2) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *ibid.*, **83**, 3986 (1961).
(3) J. P. Schaefer and D. S. Weinberg, *J. Org. Chem.*, **30**, 2635 (1965).
(4) (a) H. C. Brown and P. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967); H. C. Brown and W. J. Hammar, *ibid.*, **89**, 1524 (1967); (b) H. C. Brown, J. H. Kawakami, and S. Ikegami, *ibid.*, **89**, 1525 (1967).
(5) Optical rotations are $[\alpha]^{30}D$ for chloroform solutions.

tors using different batches of resolved **1**. Providing that (a) no activity is lost in any of the steps and (b) the resolution of the 1,2-dimethyl-*exo*-2-norbornyl system was complete, the rotations in the chart are absolute rotations.[6]

An independent determination of absolute rotations for the 1-methyl-*exo*-2-norbornyl system by the nmr method of Mislow and Raban[6] gave results consistent with those in Chart I. Partially resolved 1-methyl-*exo*-2-norbornanol (**2**) was esterified with excess optically pure O-methylmandelyl chloride and the ratio of the resulting diastereoisomers (which corresponds to the ratio of enantiomers in **2**) was determined by nmr spectroscopy. The chemical shifts of the α-methine proton singlet and the C-methyl singlet differ for the two diastereoisomers by 0.037 and 0.185 ppm, respectively. However, in each region there is overlap with signals due to other protons in the molecule and corrections for the superimposed absorptions are required for determining the proportions of the two diastereoisomers. An absolute rotation of about 85° for **1** was obtained by this method.

The 1,2-dimethyl-*exo*-2-norbornyl system[7] was resolved by recrystallization of the brucine salt of the acid phthalate derivative to constant rotation. The tertiary alcohol (**8**) was converted into the acid phthalate derivative (**4**) and the optically active alcohol was regenerated from the resolved acid phthalate by methods developed earlier for resolution of tertiary alcohols.[8] Evidently the resolution was complete. The maximum rotations for the acid phthalate (**4**), alcohol (**8**), and *p*-nitrobenzoate (**7**) in Chart I were reproducible and recrystallization of **4** and **7** did not result in optical fractionation; recrystallization of partially resolved **7** results in substantial optical fractionation.

Experimental Section

Analytical gas–liquid partition chromatography (glpc) was carried out with a 100-ft Ucon Polar (IB-550-X) capillary column and an operating temperature of 85°. Flame ionization detection was used and compositions are based on relative peak areas. Melting points are uncorrected and nmr spectra were determined with a Varian A-60A spectrometer. Chemical shifts are relative to tetramethylsilane.

1-Methyl-2-*exo*-norbornanol (2).—1-Methyl-2-*exo*-norbornyl acetate was prepared from norcamphor in two steps in 60% over-all yield by a previously described procedure.[2,7] In a typical experiment the acetate was saponified as follows. To a refluxing solution of 19 g of potassium hydroxide in 100 ml of methanol was added 42.8 g (0.25 mol) of the above acetate. The resulting solution was refluxed for 2 hr and then poured into 500 ml of ice and water. The mixture was saturated with sodium chloride and extracted with pentane. Removal of the pentane by distillation gave 24.3 g (76%) of residual oil which solidified on standing. This material contained 80% 1-methyl-2-*exo*-norbornanol (**2**) and about 18% a mixture of *endo*- and *exo*-2-methylnorbornanols.

Preparation and Resolution of 1-Methyl-*exo*-2-norbornyl Acid Phthalate (1).—A solution of 76.4 g (0.61 mol) of distilled 1-methyl-*exo*-2-norbornanol (**2**), bp 85–90° (10 mm), and 90.4 g (0.61 mol) of pure phthalic anhydride in 150 ml of dry pyridine (dried over potassium hydroxide and distilled and stored over barium oxide) was heated on a steam bath for 2.5 hr. After cooling, the mixture was poured onto a slurry of ice and 10% hydrochloric acid and the resulting mixture was extracted four times with methylene chloride. The extracts were combined, washed once with 10% hydrochloric acid, twice with water, and dried over magnesium sulfate. Removal of the solvent gave 157 g (94%) of crude **1** which was resolved as described below.

An analytical sample was purified by two recrystallizations from an ether–pentane mixture and had mp 114–115°.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.26; H, 6.70.

In a typical resolution 155 g (0.57 mol) of the above-described crude acid phthalate (**1**) and 167 g (0.57 mol) of cinchonine were dissolved in 520 ml of hot chloroform. The solution was filtered and mixed with 2 l. of hot ethyl acetate. The resulting solution was cooled to room temperature, diluted with 2 l. of pentane, and placed in a refrigerator for 2 days. Filtration gave a first crop of 163 g of cinchonine salt. This material was dissolved in 260 ml of hot chloroform and the resulting solution was mixed with 1 l. of ethyl acetate. After cooling to room temperature the solution was diluted with 1.5 l. of pentane and placed in an ice box. Filtration gave 106 g of white crystalline salt. The acid phthalate regenerated from this crop had $[\alpha]^{30}D$ −11.6° (*c* 5.6).[9] An additional recrystallization of the cinchonine salt from a mixture of 150 ml of chloroform, 600 ml of ethyl acetate, and 600 ml of pentane (the salt was dissolved first in the chloroform) gave 80 g of salt. The acid phthalate, regenerated by treatment with cold 3% hydrochloric acid and isolated by extraction with benzene, had $[\alpha]^{30}D$ −22.7° (*c* 6.92).[9] Additional recrystallizations of the cinchonine salt from chloroform–ethyl acetate mixtures gave material from which (−) **1**, $[\alpha]^{30}D$ −34.3° (*c* 3.0), was obtained.[10]

Optically Active 1-Methyl-2-*exo*-norbornanol (2).—In a typical experiment, a solution of 1.2 g of (−)-1-methyl-2-*exo*-norbornyl acid phthalate (**1**), $[\alpha]^{30}D$ −34.3° (*c* 3.0), in 40 ml of 10% sodium hydroxide was refluxed for 2 hr and then distilled. The distillate was saturated with sodium chloride and extracted six times with pentane. The extracts were combined, dried ($MgSO_4$) and the solvent was removed with a fractionating column. Sublimation of the solid residue gave 358 mg (65%) of (+)-1-methyl-2-*exo*-norbornanol (**2**): mp 71–71.5°; $[\alpha]^{30}D$ 0.48°; $[\alpha]^{30}_{365}$ 8.88° (*c* 5.0).[9] This material was found to be >99.4% pure by glpc.[10] Preparative glpc (20% KOH, 1% Carbowax 20M on acid-washed firebrick) gave a sample with no detectable contaminants. The nmr spectrum ($CDCl_3$) had a sharp singlet at δ 1.13 (3 H) rising from a broad envelope of unresolved absorption reaching from δ 0.8 to 2.3 and a doublet (with finer unresolved splitting) at δ 3.45 (1 H), J = 6 cps, due to the 2-*endo* proton. A sample of lower optical purity had $[\alpha]^{30}D$ −0.32° and $[\alpha]^{30}_{365}$ 3.18° (*c* 14).[9] A similar change in sign for these wavelengths was observed earlier, $[\alpha]^{25}D$ 0.21° and $[\alpha]^{25}_{365}$ −2.11°.[11]

Determination of Optical Purity of the 1-Methyl-*exo*-2-norbornyl System.—D-Mandelic acid (Aldrich Chemical Co.) was converted into optically pure (+)-O-methylmandelic acid {mp 66–67°; $[\alpha]^{30}D$ 141.5° (*c* 0.45 absolute ethanol) [lit.[12] mp 65–67°, $[\alpha]^{25}D$ 144° (*c* 1.5 absolute ethanol)]} by a method described earlier.[13] The nmr spectrum ($CDCl_3$) had singlets at δ 3.40 (3 H), 4.78 (1 H), 7.40 (5 H), and 9.9 (1 H) ppm.

The above (+)-O-methylmandelic acid (1 g, 0.006 mol) was heated at 70° for 1.5 hr with 0.22 ml (0.0025 mol) of phosphorus trichloride. The viscous solution was cooled, divided into two parts, and added to solutions of 100 mg each of L-menthol and partially resolved 1-methyl-*exo*-norbornanol (**2**) in 5 ml of dry pyridine. This is about a fivefold excess of the acid chloride. The reaction mixtures were stirred for 30 min, dissolved in benzene, and the resulting solution was washed successively with cold dilute hydrochloric acid, sodium carbonate solution, and water and dried over sodium carbonate. The solvent was removed under reduced pressure and the nmr spectra of the residual esters were taken.

The nmr spectrum of the L-menthol derivative in benzene had a sharp single peak for the mandelate methine proton which

(6) M. Raban and K. Mislow in "Topics in Stereochemistry," Vol. 2, N. L. Allinger and E. L. Eliel, Ed., John Wiley & Sons, Inc., New York, N. Y., 1967, p 199.

(7) H. Toivonen, *Suoman Kemistliehti, B*, **33**, 66 (1960).

(8) W. von E. Doering and H. H. Zeiss, *J. Amer. Chem. Soc.*, **72**, 147 (1950); H. H. Zeiss, *ibid.*, **73**, 2391 (1951).

(9) Optical rotations are for chloroform solutions unless noted otherwise.

(10) Infrared and nmr spectra and glpc retention times of the active sample were indistinguishable from those of an authentic racemic sample.

(11) J. A. Berson, J. H. Hammons, A. W. McRowe, R. G. Bergmann, A. Remanick, and D. Houston, *J. Amer. Chem. Soc.*, **89**, 2590 (1967).

(12) J. Jacobus, M. Raban, and K. Mislow, *J. Org. Chem.*, **33**, 1142 (1968).

(13) W. A. Bonner, *J. Amer. Chem. Soc.*, **73**, 3126 (1951).

establishes that only one diastereoisomer was present (the chemical shift difference for the methine signal in the diastereoisomers is 4.0 Hz for a 60-MHz spectrum). This shows that the above O-methylmandelyl chloride was optically pure.[6]

The two diastereoisomers resulting from esterification of racemic 1-methyl-2-*exo*-norbornanol with DL-O-methylmandelyl chloride show different chemical shifts for the C-methyl singlet and the mandelate methine singlet. In benzene, the C-methyl singlets differ by 0.187 ppm (δ 0.848 and 1.035) and the mandelate methine singlets differ 0.037 ppm (δ 4.660 and 4.697). However, in each region there is overlap with absorption due to other protons. The upfield mandelate methine signal overlaps with the lower broad peak of the C_2-*endo* proton doublet. For this reason, and the fact that the two methine signals are not completely separated, the proportions of the two diastereoisomers can not be determined accurately from the relative intensities of these absorptions. The C-methyl signals are also superimposed to different extents on other absorption. As a result, the ester derived from racemic **2** (equal amounts of the two diastereoisomers) has an nmr spectrum in which the downfield C-methyl signal has a larger area above a reference line than the upfield signal. The ratio of these areas was about 0.78.

The optical purity of the O-methyl mandelate ester derived from partially resolved **1** and optically pure O-methylmandelyl chloride was estimated from the relative areas of the two C-methyl singlets. The observed ratio of areas was multiplied by 0.78 to correct for the unequal superimposed absorption and the optical purity was calculated from the corrected relative intensities in the usual manner.[6] In this manner optically active **2** derived from (+) **2**, $[\alpha]^{30}D$ 19.4°, was found to be about 22% optically pure and active **2** derived from (−) **2**, $[\alpha]^{30}D$ −34.3°, was found to be about 43% optically pure. These results correspond to absolute rotations for **1** of 88 and 80°, respectively.

Conversion of (+)-1-Methyl-2-*exo*-norbornanol (2) into (−)-1-Methyl-2-norbornanone (3).—Oxidation of 5.62 g of (+) **2**, derived from acid phthalate derivative (**1**) having $[\alpha]^{30}D$ −28.3° (*c* 2.0), by chromium trioxide in pyridine by a previously described procedure,[3] gave 4.98 g (89%) of (−) **3**. After short-path distillation 4.4 g (80%) of liquid (−) **3** was obtained which was completely homogeneous (glpc) and had $[\alpha]^{30}D$ −16.42° (*c* 1.7).[9,10] Two other experiments gave values of 1.75 and 1.84 for the ratio of rotations for **1** and **3** compared with 1.72 for the above experiment. An average value of 1.77 was used for the correlation in Chart I.

Conversion of (−)-1-Methyl-2-norbornanone (3) into (−)-1-Methyl-2-methylenenorbornane (5) and (+)-1,2-Dimethyl-2-*endo*-norbornanol (6).—To a suspension of 18 g (0.05 mol) of methyltriphenylphosphonium bromide in 150 ml of ether under a dry nitrogen atmosphere was added 25 ml of butyllithium (22% by weight) in hexane. To the resulting yellow mixture was added 4.4 g (0.04 mol) of (−)-1-methyl-2-norbornanone (**3**), $[\alpha]^{30}D$ −16.42 (*c* 1.7), and the reaction mixture, under nitrogen, was refluxed for 68 hr. After cooling the mixture was extracted with ether and after drying ($MgSO_4$) the extract was concentrated with a Vigreux column and the residue was fractionated with a spinning-band column. A 1.5-g (34%) fraction boiling at 124–132° was collected and found to be about 80% 1-methyl-2-methylenenorbornane (**5**) by glpc. Preparative glpc (20% Ucon Polar on Chromosorb W) gave a homogeneous sample of (−) **5** that had $[\alpha]^{30}D$ −35.4°.[9,10] Another experiment gave a value of 2.07 for the ratio of rotations of **5** and **3** compared with 2.16 or the above experiment.

(−)-1-Methyl-2-norbornanone, $[\alpha]^{30}D$ −10.20° (*c* 3.1), was converted into (+)-1,2-dimethyl-*endo*-2-norbornanol (**6**) in 65% yield by reaction with methylmagnesium bromide in the usual manner. A pure sample of (+) **6** was obtained by preparative glpc (30% cyanosilicone on Chromosorb W) and had mp 42–45°, $[\alpha]^{30}D$ 0.43.[9,10]

Conversion of (−)-1-Methyl-2-methylenenorbornane (5) into (+)-1,2-Dimethyl-*exo*-2-norbornanol (8).—Oxymercuration–demercuration of (−) **5**, $[\alpha]^{30}D$ −10.68° (*c* 3.5), according to a previously described procedure[4a] gave (+) **8**. After purification by preparative glpc (20% KOH, 1% Carbowax on acid-washed firebrick) and sublimation, the product had $[\alpha]^{30}D$ 2.27° (*c* 4.5).[9,10]

In another experiment (+) **5**, $[\alpha]^{30}D$ 10.8 (*c* 4.7), gave (−) **8**, $[\alpha]^{30}D$ −2.32° (*c* 10).

Preparation and Resolution of 1,2-Dimethyl-*exo*-2-norbornyl Acid Phthalate (4).—1,2-Dimethyl-*exo*-2-norbornanol (**8**) was prepared in four steps from 1-methyl-2-norbornanone (**3**)[2] by the procedure of Toivonen.[7] The over-all yield was 83% and after sublimation from potassium hydroxide the product was >95% pure, mp 104–106° (lit.[7] mp 112–113°). The contaminants were 1,2-dimethyl-*endo*-2-norbornyl chloride (4%) and 1-methyl-*endo*-2-norbornanol.

The tertiary alcohol, **8**, was converted into the acid phthalate derivative as follows. Finely divided potassium, 33.2 g (0.85 mol), in 750 ml of tetrahydrofuran (purified by distillation from $LiAlH_4$ prior to use) was prepared by vigorous stirring of the refluxing mixture under nitrogen. To this stirred mixture, 119 g (0.85 mol) of **8** in 300 ml of dry tetrahydrofuran was added dropwise as the reaction mixture was blanketed with nitrogen. The mixture was stirred at reflux for an additional 4 hr, chilled to −78°, and a solution of 119 g (0.80 mol) of pure phthalic anhydride in 1.3 l. of dry tetrahydrofuran was added dropwise over a period of 1 hr. The resulting mixture was stirred under nitrogen at −78° for 10 hr. After warming to room temperature, water was added to dissolve the precipitated potassium salts and most of the tetrahydrofuran was removed with a rotary evaporator. The concentrated reaction mixture was acidified with excess cold 10% hydrochloric acid and extracted with a 1 l. and two 500-ml portions of benzene. After drying ($MgSO_4$), most of the solvent was removed under reduced pressure and pentane was added to the residual oil to initiate crystallization. Recrystallization of the crude product from ether–pentane gave 171 g (74% yield) of acid phthalate (**4**), mp 130–132 (with resolidfication due to decomposition). A neutral equivalent showed that this product contained less than 2% phthalic acid. An analytical sample was prepared by recrystallization from chloroform–pentane.

Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.81; H, 7.08.

The above acid phthalate (**4**) was resolved as follows. To a warm solution of 233 g (0.59 mol) of brucine in 510 ml of acetone was added 170 g (0.59 mol) of **4**. After solution was complete 160 ml of water was added and the solution was chilled in a refrigerator for 2 days after which 95 g of brucine salt was collected. A small sample was converted into the acid phthalate derivative, (+) **4**, $[\alpha]^{30}D$ 6.2 (*c* 2),[9,14] by hydrolysis with cold 1% hydrochloric acid.

The first crop of brucine salt was recrystallized by dissolving it in about 400 ml of acetone, concentrating to about 90 ml, adding 15 ml of water and placing the resulting clear solution in an icebox. After six additional recrystallizations the head crop, 12 g, was converted into (+) **4**: mp 121–122°, neut equiv 289 (theory 288), $[\alpha]^{30}D$ 7.85° (*c* 1.86).[10,14] The mother liquor from the last recrystallization of the brucine salt was evaporated and the residue, 3 g, was converted into (±) **4** which had the same rotation as the (+) **4** derived from the head crop. This shows that the salt was recrystallized to constant rotation. Another resolution gave (+) **4** with the same maximum optical rotation.

Optically Active 1,2-Dimethyl-*exo*-2-norbornanol (8) and Derivatives (7 and 9).—The above (+) **4** (4 g) was converted into (−) **8** by reduction with $LiAlH_4$.[8] The crude product, 1.05 g (52%), was purified by preparative glpc (10-ft column, 20% KOH and 1% Carbowax 20M on firebrick). The (−) **8** obtained in this manner was >99.9% pure (glpc) and had mp 104–105.5°, $[\alpha]^{30}D$ −22.59°, $[\alpha]^{30}_{365}$ −85.93° (*c* 7.33).[10] This maximum rotation was also observed in another resolution.

The above optically pure (−) **8** was converted into the *p*-nitrobenzoate derivative, (+) **7**, with *p*-nitrobenzoyl chloride by the procedure used for preparation of the acid phthalate derivative except that the reaction period at −78° was 5 hr instead of 10 hr and the solution was not acidified during the isolation of the product. After one recrystallization from ether–pentane a 69% yield of (+)-1,2-dimethyl-*exo*-2-norbornyl *p*-nitrobenzoate was obtained which had mp 142–143°, $[\alpha]^{30}D$ 37.3°, $[\alpha]^{30}_{463}$ 73.8° (*c* 5.5).[10] After three additional recrystallizations (+) **7** had mp 143–144° and the same rotations as above which indicates that this material was optically pure.[15]

(14) The rotation of optically active **4** in chloroform is very sensitive to temperature and concentration, *e.g.*, optically pure (+)-**4** has $[\alpha]^{30}D$ 7.07° (*c* 2.2) and $[\alpha]^{30}D$ 3.39° (*c* 13.1). The rotation of optically active **1** in chloroform is insensitive to change in concentration from *c* 0.6 to 20.

(15) Three recrystallizations of partially resolved **7** changed the rotation[5] from 21.7 to 26.8°.

Anal. Calcd for $C_{16}H_{19}O_4N$: C, 66.42; H, 6.62; N, 4.84. Found: C, 66.66; H, 6.53; N, 4.71.

A sample of (−) **8**, $[\alpha]^{30}$ −21.73° (*c* 8.0) (96% optically pure), was converted into the methyl ether, (+) **9**, as follows. (−) **8**, 200 mg (1.43 mmol), was converted into the potassium salt in 10 ml of tetrahydrofuran as described above for preparation of the acid phthalate derivative. To the stirred solution at room temperature under nitrogen was added 170 mg (1.20 mmol) of methyl iodide in 5 ml of tertrahydrofuran. The mixture was stirred at room temperature for 1 hr, 1 ml of water was added, and the solution was concentrated under reduced pressure. The residue was shaken with a mixture of 15 ml of pentane and 15 ml of water. The organic layer was separated, dried ($MgSO_4$), and the pentane removed with a fractionation column. The residue was purified by preparative gc (20-ft column, 30% Carbowax 20M on Chromosorb at 150°). The yield was 122 mg (55%) and (+) **9** was >99.4% pure (glpc) and had $[\alpha]^{30}D$ 33.27° (*c* 10.0). Presumably this material is 96% optically pure.

Anal. Calcd for $C_{10}H_{18}O$: C, 77.86; H, 11.76. Found: C, 77.99; H, 11.75.

Registry No.—(−) **1**, 18366-92-2; (+) **2**, 16651-55-1; (+) **4**, 18366-94-4; (−) **5**, 18366-95-5; (+) **6**, 18366-96-6; (+) **7**, 18366-97-7; (−) **8**, 18366-98-8; (+) **9**, 18366-99-9.

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Nitrilium Salts. A New Method for the Synthesis of Secondary Amines[1]

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A new method for the synthesis of secondary amines is described involving the sodium borohydride reduction of imino esters prepared from nitrilium salts. This conversion of nitriles into secondary amines proceeds in high yield and has been applied to a variety of compounds. The nitrilium salts are easily prepared from nitriles and dialkoxycarbonium fluoroborates (**5**), which are readily available from the corresponding ortho esters. Although most of the compounds examined gave the corresponding secondary amines as exclusive products, alkylation with di-*n*-propoxycarbonium fluoroborate (**5c**) gave the rearranged isopropylamine as the major product. The mechanism of the over-all reaction is discussed in light of intermediates observed, and a mechanism for the rearrangement is suggested.

Although nitrilium salts have been known for some time, little is known about the chemistry of these compounds. N-Ethylnitrilium salts (**2**) have been synthesized by reaction of nitriles with triethyloxonium fluoroborate[2] and with diethoxycarbonium hexachloroantimonate.[3] The powerful electrophilicity of these salts has been demonstrated[2] by their instantaneous conversion to amides upon treatment with water. Although there are numerous methods available for the synthesis of amines,[4] the conversion of a nitrile into a secondary amine requires vigorous reducing conditions which preclude selective reduction with other easily reduced functional groups present. Our need for such a selective method for the conversion of a nitrile into a secondary amine for a total synthesis currently under investigation prompted us to examine the reduction of these nitrilium salts.

Initial efforts were directed toward the synthesis of N-ethylnitrilium salts based on Meerwein's procedure[2] and the subsequent reduction of these salts by metal hydrides. The nitrilium salts (**2**) were readily prepared by refluxing the nitrile and 2 equiv of triethyloxonium fluoroborate in methylene chloride; reaction of **2** with absolute ethanol, followed by treatment with sodium borohydride in methanol at 0° or in ethanol at 25°, afforded good yields of the corresponding secondary amine (**4**) (Scheme I). The nitrilium salt is rapidly converted into imino ester **3** which undergoes slow reduction to the secondary amine. The reaction proceeds well for aromatic nitriles and for primary-, secondary-, and tertiary-substituted aliphatic nitriles.[1a]

SCHEME I

$$\underset{\mathbf{1}}{RC{\equiv}N} + Et_3O^+BF_4^- \text{ or } \mathbf{5b} \xrightarrow[\text{reflux}]{CH_2Cl_2} \underset{\mathbf{2}}{RC{\equiv}\overset{+}{N}CH_2CH_3\,BF_4^-} \xrightarrow[\text{fast}]{EtOH} \underset{\mathbf{3}}{RC(OEt){=}NCH_2CH_3} \xrightarrow[\text{slow}]{NaBH_4} \underset{\mathbf{4}}{RCH_2NHCH_2CH_3}$$

R = −Ph, −CH_2Ph, −$CHPh_2$, −$(CH_2)_3CH_3$, −$CH(CH_3)_2$, −$C(CH_3)_3$

Attention was then directed to the synthesis of nitrilium salts other than the N-ethyl compounds. Because of the difficulties which Meerwein encountered in the preparation of trialkyloxonium fluoroborates containing groups larger than ethyl,[5] we turned to a modification of Meerwein's method[6] for the preparation of diethoxycarbonium fluoroborate (**5b**) in the hope that other dialkoxycarbonium fluoroborates could be made from other ortho esters. Thus **5b** was prepared by reaction of triethyl orthoformate with boron trifluoride etherate at −30° in methylene chloride; this compound proved to be an efficient ethylating agent for nitriles and afforded yields of secondary amines comparable with those obtained with triethyloxonium fluoroborate.

Our hope that the alkylating species could be varied

(1) (a) A preliminary report of this work has appeared: R. F. Borch, *Chem. Commun.*, 442 (1968). (b) Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., March 31–April 5, 1968.

(2) H. Meerwein, P. Laasch, R. Mersch, and J. Spille, *Chem. Ber.*, **89**, 209 (1965).

(3) S. Kabuss, *Angew. Chem. Intern. Ed. Engl.*, **5**, 675 (1966).

(4) For a general reference, see Houben Weyl's "Methoden der organischen Chemie," Vol. XI, Part I, G. Thieme Verlag, Stuttgart, 1957.

(5) H. Meerwein, E. Battenberg, H. Gold, E. Pfeil, and G. Willfang, *J. Prakt. Chem.*, **154**, 83 (1939).

(6) H. Meerwein, K. Bodenbenner, P. Borner, F. Kunert, and K. Wunderlich, *Ann.*, **632**, 38 (1960).